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Gary Brian Evans

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EXAMINER

MOORE, SUSANNA

ART UNIT

PAPER NUMBER

1624

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PAPER

**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

<b>Office Action Summary</b>	<b>Application No.</b> 10/524,995	<b>Applicant(s)</b> EVANS ET AL.	
	<b>Examiner</b> SUSANNA MOORE	<b>Art Unit</b> 1624	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

### Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

### Status

- 1) ☒ Responsive to communication(s) filed on 11 January 2008.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

### Disposition of Claims

- 4) ☒ Claim(s) 1-9, 11-18, 20-25, 27 and 29-31 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 1-9, 11-18, 20-22, 24, 25 and 27 is/are rejected.
- 7) ☒ Claim(s) 23 and 29-31 is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

### Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

### Priority under 35 U.S.C. § 119

- 12) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☒ All b) ☐ Some \* c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
  - ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  - ☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

### Attachment(s)

- |  |   |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892)                       | 4) <input type="checkbox"/> Interview Summary (PTO-413)           |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)   | Paper No(s)/Mail Date. _____                                      |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date <u>1/11/08</u> .   | 6) <input type="checkbox"/> Other: _____                          |

## **DETAILED ACTION**

### ***Response to Arguments***

Applicant's arguments, see Remarks, filed 1/11/2008, with respect to the Office Action mailed 9/11/2007 have been fully considered. This is a Final Office Action. In summary, claims 1-9, 11-18, 20-25 and 29-31 are currently pending and under consideration. Claims 29-31 are new claims.

### ***Claim Objections***

Claims 23 and 29-31 are objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

### ***Specification***

The objection to the title of the invention for not being descriptive is withdrawn based on the new title submitted.

### ***Claim Rejections - 35 USC § 112***

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

The rejection of claims 25-28 under 35 U.S.C. 112, second paragraph, as being indefinite for the specification not setting forth any steps involved in determining how to identify “a disease or condition in which it is desirable to inhibit purine phosphoribosyltransferase, purine nucleoside phosphorylase, 5'-methylthio adenosine phosphorylase, 5'-methylthioadenosine nucleosidase and/or nucleoside hydrolase” is withdrawn based on the amendments.

Claim 27 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The term “arthritis” is indefinite. By itself, it is not a standard medical term for a specific disease or groups of related diseases, but a general term denoting inflammation of the joints, and may or may not involve inflammation of other parts of the body such as the nails. It mostly commonly refers to any of osteoarthritis, gouty arthritis, or rheumatoid arthritis. These are three totally different and unrelated disorders, which all have “arthritis” in their name and involve inflammation of the joints.

Applicant states, “Accordingly, applicants maintain that the metes and bounds of the claim are clear and thus reconsideration and withdrawal of this rejection are respectfully requested.”

This is not persuasive. Thus, the rejection is maintained.

Claims 1-9, 11-18, 20-22, 24, 25 and 27 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. In claim 1, Applicants have the limitations "optionally substituted alkyl, aralkyl or aryl group". Substituted by what? Nowhere in the specification are these possible substituents listed.

Applicant states, "Applicants note that an optional substituent in variable Q can be found at least in the Tables on pages 19 and 55 of the specification. In addition, examples of substituents can be found in Formula (I), Formula (II) and Formula (III). Applicants maintain that one of ordinary skill in the art can determine that an alkyl, aralkyl or aryl group is substituted and thus that the metes and bounds of the claim are clear."

This is not persuasive because the support to which Applicant refers only gives support for those particular compounds, not all compound embraced by the genus of formula (I) and (II). Thus, the rejection is maintained.

The rejection of claim 24 under 35 U.S.C. 112, second paragraph, as being incomplete for omitting an essential element is withdrawn based on the amendment.

The rejection of claim 27 under 35 U.S.C. 112, second paragraph, as being indefinite for the term "transplant rejection" is withdrawn.

Claims 1-9, 11-18, 20, 21, 24, 25 and 27 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject

matter which applicant regards as the invention. Claim 1 recites the limitation "CH" in the definition for E. There is insufficient antecedent basis for this limitation in the claim.

The rejection of claims 1-9, 11-18 and 20-28 under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for making salts of the claimed compounds, does not reasonably provide enablement for making esters or prodrugs is withdrawn based on the amendments.

Claims 25 and 27 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter, which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. Such a utility cannot be deemed enabled?

Pursuant to *In re Wands*, 858 F.2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988), one considers the following factors to determine whether undue experimentation is required: (A) The breadth of the claims; (B) The nature of the invention; (C) The state of the prior art; (D) The level of one of ordinary skill; (E) The level of predictability in the art; (F) The amount of direction provided by the inventor; (G) The existence of working examples; and (H) The quantity of experimentation needed to make or use the invention based on the content of the disclosure. Some experimentation is not fatal; the issue is whether the amount of experimentation is “undue”; see *In re Vaeck*, 20 USPQ2d 1438, 1444.

**The analysis is as follows:**

**(A) Breadth of claims.**

**(a) Scope of the compounds.** The instant claims encompass thousands of compounds with a pyrrolo[3,2-d]pyrimidine scaffold with a variety of substituents at four positions.

**(b) Scope of the diseases covered.** The instant claims are drawn to a method of treating a subject having a disease or condition in which it is desirable to inhibit purine phosphoribosyltransferase, purine nucleoside phosphorylase, 5'-methylthio adenosine phosphorylase, 5'-methylthioadenosine nucleosidase and/or nucleoside hydrolase wherein the disease or condition is a cancer, bacterial infection, protozoal infection, and T-cell mediated, e.g. psoriasis or arthritis, and transplant rejection. The claim thus covers both treatment of diseases and simultaneous inhibition.

Cancers are classified by the type of cell that resembles the tumor and, therefore, the tissue presumed to be the origin of the tumor. The following general categories are usually accepted:

- Carcinoma: malignant tumors derived from epithelial cells.
- Lymphoma and Leukemia: malignant tumors derived from blood and bone marrow cells
- Sarcoma: malignant tumors derived from connective tissue, or mesenchymal cells.
- Mesothelioma: tumors derived from the mesothelial cells lining the peritoneum and the pleura.
- Glioma: tumors derived from glia, the most common type of brain cell.
- germ cell tumours: tumors derived from germ cells, normally found in the testicle and ovary.
- Choriocarcinoma: malignant tumors derived from the placenta.

Cancers include the following, but are not limited to: (topography) eye, endometrium,

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bladder, breast, colon, penis, kidney, liver, lung, brain, small cell lung cancer, esophagus, gall bladder, ovary, pancreas, stomach, cervix, colon/rectum, mouth, larynx, head/neck, thyroid, prostate, testicle, skin, squamous cell carcinoma, anus and leukemia; (cell type/morphology) acute lymphocytic leukemia, acute lymphoblastic leukemia, B-cell lymphoma, T-cell lymphoma, Hodgkins lymphoma, non-Hodgkins lymphoma, hairy cell lymphoma, Burgett's lymphoma, acute myelogenous leukemia, chronic myelogenous leukemia, myelodysplastic syndrome, promyelocytic leukemia, fibrosarcoma, rhabdomyosarcoma, astrocytoma, neuroblastoma, glioma, schwannomas, melanoma, seminoma, teratocarcinoma, osteosarcoma, xenoderoma pigmentosum, keratoanthoma, thyroid follicular cancer, Kaposi's sarcoma, angiosarcoma, dermatofibrosarcoma, desmoid tumor, desmoplastic small round cell tumor, extraskeletal chondrosarcoma, extraskeletal osteosarcoma, hemangiopericytoma, hemangiosarcoma, leiomyosarcoma, liposarcoma, lymphangiosarcoma, malignant fibrous histiocytoma, neurofibrosarcoma, synovial sarcoma, Askin's Tumor, Ewing's sarcoma and malignant hemangioendothelioma.

Next, T-cell mediated disease encompass inflammatory and autoimmune diseases among many others.

An inflammatory disease can be defined as a disease characterized by inflammation anywhere in the body. Inflammation is the body's first response to injury, e.g. trauma, infection irritation, etc. This is a non-specific immune response. Inflammation has two main components - cellular and exudative.



The exudative component involves the movement of fluid, usually containing many important proteins such as fibrin and immunoglobulins (antibodies). Fibrinogen is important for clot formation and the prevention of further loss of blood. Immunoglobulins may act as specific or nonspecific *opsonins* facilitating thus the process of phagocytosis, or may participate in antibody-dependent cell-mediated cytotoxicity (ADCC) by which target cells are destroyed by killer cells. Blood vessels are dilated upstream of an infection (causing redness and heat) and constricted downstream while capillary permeability to the affected tissue is increased, resulting in a net loss of blood plasma into the tissue - giving rise to edema or swelling. The swelling distends the tissues, compresses nerve endings, and thus causes pain.

The cellular component involves the movement of white blood cells from blood vessels into the inflamed tissue. Professional phagocytes (neutrophils, eosinophils, monocytes and tissue macrophages) are essential performing phagocytosis, lymphocytes are involved in the specific immune responses, endothelial cell in the regulation of leukocyte emigration from the blood into inflamed tissue and platelets with mast cells in the production of early phase mediators.

For the possibility of surrounding tissue damage, inflammatory responses must be well ordered and controlled. The body must be able to act quickly in some situations, for example to reduce or stop the loss of blood, whereas tissue repair and reconstruction can begin a little later. Therefore, a wide variety of interconnected cellular and humoral (soluble) mechanisms are activated when tissue damage and infection occur. The body has the capacity to respond to both minor injuries such as bruising, scratching, cuts, and abrasions, as well as to major injuries such as severe burns and amputation of limbs.

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Some examples of inflammatory diseases are as followed, but not limited to: allergies, appendicitis, arteritis, arthritis, asthma, blepharitis, bronchiolitis, bronchitis, bursitis, cervicitis, cholangitis, cholecystitis, chorioamnionitis, colitis, conjunctivitis, cystitis, dacryoadenitis, dermatitis, dermatomyositis, encephalitis, endocarditis, endometritis, enteritis, enterocolitis, epicondylitis, epididymitis, fasciitis, fibrositis, gastritis, gastroenteritis, gingivitis, hepatitis, hidradentitis supparativa, ileitis, immune reconstitution inflammatory syndrome (IRIS), laryngitis, mastitis, meningitis, myelitis, myocarditis, myositis, nephritis, omphalitis, oophoritis, orchitis, osteitis, otitis, pancreatitis, parotitis, pelvic inflammatory disease (PID), pericarditis, peritonitis, pharynx, pleuritis, phlebitis, pneumonitis, protitis, prostatitis, rhinitis, salpingitis, sinusitis, stomatitis, synovitis, tendonitis, tonsillitis, uveitis, vaginitis, vasculitis and vulvitis.

Arthritis is a general term for inflammation of the joints via any process. Arthritic diseases include rheumatoid arthritis, which is an autoimmune diseases; infectious arthritis, caused by joint infection; psoriatic arthritis, gouty arthritis, caused by uric acid crystals; and the more common osteoarthritis, or degenerative joint disease. Arthritis can be caused from strains and injuries from repetitive motion, sports, overexertion and falls. Unlike the autoimmune diseases, osteoarthritis largely affects older people, and results from the degeneration of joint cartilage. Some other forms of arthritis are, but not limited to: juvenile arthritis, Still's disease and ankylosing spondylitis

The immune system is the body's defense against infectious organisms and other invaders. Through a series of steps called the immune response, the immune system attacks

antigens, which are not recognized by the body, and are destroyed by the immune system.

The immune system is made up of a network of cells, tissues, and organs that work together to protect the body. The key organs of the immune system are thymus, spleen, bone marrow, lymph vessels, lymph nodes and secondary lymphatic tissues such as tonsils, adenoids, and skin.

The immune system is often divided into two sections. One being innate immunity which is comprised of hereditary (always there) components that provide an immediate "first-line" of defense to continuously ward off pathogens.

The second is adaptive immunity, which is triggered when an antigen is detected. Several types of cells work together to recognize and respond to it. These cells trigger the B lymphocytes to produce antibodies. Antibodies are specialized proteins that lock onto specific antigens. Antibodies and antigens fit together like a key and a lock. Although antibodies can recognize an antigen and lock onto it, they are not capable of destroying it without help. That is the job of the T cells. The T cells are part of the system that destroys antigens that have been tagged by antibodies or cells that have been infected or somehow changed.

Sometimes a person is born with an overzealous immune system. When this occurs the immune system is intact and present but not working properly. In these cases, the immune system fails to properly distinguish between self and non-self, and attacks a part of the the body. Diseases which are associated with this type of disorder of the immune system are called autoimmune disorders.

Some examples of autoimmune disorders are as follows, but not limited to: acute

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disseminated encephalomyelitis (ADEM), Addison's disease, antiphospholipid, aplastic anemia, autoimmune hepatitis, Coeliac disease, Crohn's disease, type I diabetes mellitus, Goodpasture's syndrome, Graves' disease, Guillain-Barré syndrome (GBS), Hashimoto's disease, lupus erythematosus, multiple sclerosis, myasthenia gravis, opsoclonus myoclonus syndrome (OMS), optic neuritis, Ord's thyroiditis, pemphigus, primary biliary cirrhosis, psoriasis, rheumatoid arthritis, Reiter's syndrome, Takayasu's arteritis, temporal arteritis, warm autoimmune hemolytic anemia and Wegener's granulomatosis.

**(B) The nature of the invention and predictability in the art:** The invention is directed toward medicine and is therefore physiological in nature. It is well established that “the scope of enablement varies inversely with the degree of unpredictability of the factors involved,” and physiological activity is generally considered to be an unpredictable factor. See *In re Fisher*, 427 F.2d 833, 839, 166 USPQ 18, 24 (CCPA 1970).

**(C) Direction or Guidance:** That provided is very limited. The dosage range information, found on page 22 of the Specification gives 0.1-100 mg/kg, which is broad. Moreover, this is generic, the same for the many disorders covered by the specification. Thus, there is no specific direction or guidance regarding a regimen or dosage effective specifically for any and all diseases found in the Scope of diseases listed above.

**(D) State of the Prior Art:** These compounds are substituted pyrrolo[3,2-d]pyrimidines with a particular substitution on the bicyclic core. So far as the examiner is aware, no substituted pyrrolopyrimidines with any substitution pattern have been used for inhibiting or treating any

and all the diseases found above under the Scope of diseases.

The state of the clinical arts in using PNPase inhibitors is that the only such inhibitor ever tested in the clinic is BCX-34. According to Anonymous (BioCryst News) that compound failed in a clinical trial for psoriasis treatment. BCX-34 has also failed as a sole agent for the treatment of AIDS. Thus, not even the most educated and experienced one would know how to use a PNPase inhibitor clinically.

**(E) Working Examples:** The invention is drawn to a method of treating cancer, bacterial infection, protozoal infection and T-cell mediated diseases. There are working examples on pages 16-21 drawn to the inhibition of hMTAP, *mycobacterium tuberculosis* PNP, *plasmodium falciparum* PNP, hPNP and *E. coli*. MTAN, only. **There are no assays drawn to the inhibition of any PPRTs.** The pharmacological assays are described on pages spanning 57-60. The assays consist of an *in vitro* assay using PNP, *in vitro* assays of the inhibition of MTAP and inhibition of mouse MTAP *in vivo*. **There is no description of pharmacological assays for MTANs, bacteria or protozoans.** Furthermore, there are no animal models drawn to the utility of treating any of the diseases covered by Scope to support the use of substituted pyrrolo[3,2-d]pyrimidines. The assays presented do not provide any animal data to support the treatment of cancer, bacterial infections, protozoal infections and T-cell mediated diseases.

**(F) Skill of those in the art:** The diseases and disorders disclosed in the Scope of diseases above cannot be treated generally by any one drug. These are all different diseases, which occur at different locations and by different modes of action in the body.

The prior art knows that there never has been a compound capable of treating cancer

generally. "The cancer therapy art remains highly unpredictable, and no example exists for efficacy of a single product against tumors generally."

(<<http://www.uspto.gov/web/offices/pac/dapp/lpecba.htm#7>

<[>> ENABLEMENT DECISION](http://www.uspto.gov/web/offices/pac/dapp/lpecba.htm)

TREE, Example F, situation 1) There are compounds that treat a modest range of cancers, but no one has ever been able to figure out how to get a compound to be effective against cancer generally, or even a majority of cancers. Thus, the existence of such a "silver bullet" is contrary to our present understanding in oncology.

The prior art knows that mediation of inflammation is among the most pervasive and complex of all body process. There are complex interactions among just the cytokines, and just in certain types of inflammatory responses. As a second example, the Hageman factor is a protein that initiates three different processes: a) the intrinsic clotting process, which operates via thrombin and fibrin, b) the fibrinolytic system which produces fibrinolysis via plasmin and 3) the kallikrein/kinin cascade, which produces the kinins, e.g. bradykinin. Further, Plasmin can also activate C3 and C5 in the complement cascade (an entirely separate set of vascular events) producing C3a and C5a, respectively, as can thrombin.

Further, the prior art knows that there are many paradoxical features in the inflammation system. As an example, in lung inflammation, nitric oxide appears to be a pro-inflammatory mediator in acute situations e.g. ARDS but anti-inflammatory in more stable situations. As a second example, the cytokine TGF-beta-1 possesses both pro-inflammatory and anti-inflammatory activities. Virtually all cells have TGF-beta-1 receptors, and the cytokine has many

other roles other than in inflammation. As a third example, CRF appears to have both pro-inflammatory and anti-inflammatory activities.

Thus, the prior art knows that, treatments for inflammation are normally tailored to the particular type of inflammation present, as there is no, and there can be no "magic bullet" against inflammation generally.

**(G) The quantity of experimentation needed:** Owing especially to factors A, C, E and F, the amount of experimentation is expected to be high.

MPEP 2164.01(a) states, "A conclusion of lack of enablement means that, based on the evidence regarding each of the above factors, the specification, at the time the application was filed, would not have taught one skilled in the art how to make and/or use the full scope of the claimed invention without undue experimentation. *In re Wright*, 999 F.2d 1557,1562, 27 USPQ2d 1510, 1513 (Fed. Cir. 1993)." That conclusion is clearly justified here.

Applicant states, "Applicants maintain that the teaching of the specification is enabling for the skilled artisan to practice the invention of Claim 25 without undue experimentation. Claim 27 further limits Claim 25."

This is not found persuasive. Thus, the rejection is maintained.

The rejection of claim 28 for the “use of a compound” is withdrawn based on the cancellation of said claim.

The rejection of claim 28 under 35 U.S.C. 101 for the claimed recitation of a use, is withdrawn based on the amendment.

### ***Double Patenting***

The provisional rejection of claims 1-9, 11-18, 20-23 and 28, rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claim 14 of copending Application No. 10543380 is withdrawn based on the cancellation of claim 14 from the copending Application.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.



***Conclusion***

Any inquiry concerning this communication or earlier communications from the examiner should be directed to SUSANNA MOORE whose telephone number is (571)272-9046. The examiner can normally be reached on M-F 8:00-5:00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James Wilson can be reached on (571) 272-0661. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Susanna Moore/  
Examiner, Art Unit 1624

/Brenda L. Coleman/  
Primary Examiner, Art Unit 1624